list

ATTACHMENT F
Evaluation of PCB Dermal Absorption Factor Used in HHRA

In the Human Health Risk Assessment (HHRA) for the Housatonic River, EPA has used an absorption factor of 14 percent to evaluate dermal exposure to PCBs. This dermal absorption factor is based on a study by Wester et al. (1993) of PCB absorption from the soil into the skin of Rhesus monkeys. As discussed below, that study used soil with a large particle size and very low organic carbon content, which are not typical of floodplain soils, including those in the Housatonic River floodplain, and also used PCB mixtures different from the predominant mixture found at this site. Theoretical considerations and empirical data suggest that the dermal absorption factor estimated by Wester et al. (1993) almost certainly overstates absorption of PCBs from soils and sediments at this site. Indeed, a more recent dermal absorption study by Mayes et al. (2002), employing the same general protocol as Wester et al. (1993) but using soil with a more typical particle size and organic carbon content, as well as Aroclor 1260 (the predominant PCB mixture at this site), reported dermal absorption of around 4 percent. Although both studies have limitations, GE believes that the Mayes et al. (2002) results are more representative of site-specific soils at this site and thus should be used as the basis for the dermal absorption factor in the HHRA.

Theoretical and Empirical Considerations

Estimation of an overall dermal absorption fraction for PCBs in soil or sediment is highly complex, and may involve consideration of more than just the soil and skin. The highly chlorinated PCBs are lipophilic compounds that are not metabolized in skin and move through the skin by passive diffusion (Cleek and Bunge, 1993; Bunge and Cleek, 1995; Bunge et al., 1995; Potts and Guy, 1995). Demonstration of these processes is relatively recent, but has been verified *in vivo* (e.g., Kalia et al., 1996; Pirot et al., 1997, 1998). PCBs also move through soil by passive diffusion or dissolution processes that have been extensively described (Jury et al., 1983, 1984a,b,c, 1990, 1992). When soil (or sediment) containing PCBs is deposited on the skin, or is applied to skin in a laboratory experiment, the PCBs move through the soil by diffusion, through the air within the soil, partly through the water present in the soil and through the oils present on the surface of the skin. A portion of the PCBs present in soil will diffuse outwards and escape into the air. Some will diffuse towards the skin and enter the outer layer of skin, the stratum corneum, which is the principal absorption barrier to dermal absorption. Once in the stratum corneum, PCBs again move through it

by diffusion; and if the soil is removed from the skin, the PCBs may also diffuse back out again, to escape via diffusion into the air or into skin moisture or skin oils with subsequent removal.

The fraction of PCBs that is ultimately absorbed into the body will thus be dependent on the rate at which PCBs desorb from the soil by dissolving into skin moisture and oils, the rate at which their vapors can escape to the air, the resistance to absorption presented by the stratum corneum, and the amount of time during which the soil is present on the skin surface. All of these factors are subject to variability and are influenced by the physical characteristics of the soil such as particle size and organic carbon content.

In particular, a number of studies have shown the importance of organic carbon content in the processes controlling dermal absorption of lipophilic compounds such as PCBs. The organic carbon in soil is the dominant sorbent for lipophilic compounds (Scow et al., 1995). Karickhoff et al. (1979) demonstrated, and Yang et al. (1989) confirmed, that the silt and clay fractions of soil, which contain the bulk of the soil's organic carbon content (Brady, 1984), are considerably better sorbents for lipophilic compounds than the sand fraction. Roy et al. (1990) demonstrated that the dermal absorption of PCBs is strongly influenced by the percent of organic carbon in the soil, with higher organic carbon content serving to bind PCBs and reduce their bioavailability.

Methodological Considerations Associated with the Wester et al. (1993) Study

There are a number of specific methodological considerations associated with the Wester et al. (1993) study that compromise its use as a basis for deriving a dermal absorption value for use in the Housatonic River HHRA.

The Wester et al. (1993) study was designed to measure the extent to which Aroclors 1242 and 1254 would partition out of soil and be absorbed through the skin. Wester et al. (1993) added radiolabeled Aroclor 1242 and Aroclor 1254 to a fraction sieved from a California soil that originally contained 26 percent sand, 26 percent clay, and 48 percent silt. The resulting sieved soil contained soil particles ranging from 180 to 300 microns and contained 0.9 percent organic carbon content (R. Wester, personal communication). The Aroclors were mixed into this fraction to final concentrations of 44 mg/kg Aroclor 1242 and 23 mg/kg Aroclor 1254. The sand was then held against the clipped abdominal skin of adult female Rhesus monkeys for a period of 24 hours. The skin site was covered with a non-occlusive cover that permitted air and moisture to move freely to and from the

skin but retained the sand at the application site. Urine and feces were collected during the exposure period. After 24 hours, skin was washed and urine and feces were periodically collected and analyzed for PCBs for 34 days following exposure. Percutaneous absorption was determined by urinary and fecal excretion of radiolabel following topical application. Based on their measured recoveries, combined with excretion efficiency data from intravenous studies previously conducted at their laboratory, Wester et al. (1993) concluded that the percutaneous absorption of Aroclors 1242 and 1254 from soil was 13.8 percent and 14.1 percent of applied dose, respectively.

While the experimental methodology used by the Wester et al. (1993) study was appropriate to the study's goal, there are several aspects of the experiment that limit its usefulness as a basis for extrapolating a dermal absorption factor for use in the HHRA:

- Wester et al. (1993) evaluated a sieved sand fraction with a particle size of 180 to 300 microns, thus omitting all the clay and most of the silt in the original soil. This fraction had an organic carbon content of 0.9 percent (Dr. R. Wester, personal communication), which is substantially lower than the typical levels of organic carbon found in U.S. soils (approximately 3.4 percent or greater) and in the soils and sediments of the Housatonic River and its floodplain, where the average organic carbon content in the reach between the Confluence and Woods Pond Dam is approximately 5.3 percent in the floodplain/riverbank soils (excluding vernal pools, which average over 13 percent) and approximately 4.7 percent in surface sediments (top 6 inches, including channel, backwater, and impoundment areas) (BBL and QEA, 2003). Wester et al. did not attempt to measure the dermal absorption from soils with higher (and more typical) organic carbon contents. As discussed above, both theoretical considerations and empirical data indicate that the organic carbon content of soil significantly influences the bioavailability of the PCBs in the soil, with the bioavailability decreasing as the organic carbon content increases. Thus, it is reasonable to expect that the dermal absorption values determined by Wester et al. (1993) for soils with very low organic carbon content will overestimate percutaneous absorption from soils or sediments with typical organic carbon contents, like those of the Housatonic River and floodplain.

- The Wester et al. (1993) study evaluated absorption that would occur after 24 hours of contact before washing. It is extremely unlikely that many people who get soil or sediment on their skin would wait 24 hours before washing. Even in the absence of washing, the contaminated soil on most of the skin will be removed by physical abrasion, such as by clothing (Auton et al., 1994).

In contrast, the Wester et al. (1993) study assured that the contaminated soil would remain in contact for 24 hours, by covering the skin site with a non-occlusive cover.

- Wester et al. (1993) evaluated Aroclors 1242 and 1254, but did not evaluate dermal uptake of Aroclor 1260, the predominant PCB mixture at the Housatonic River site. The chemical composition of Aroclor 1260 differs substantially from the composition of Aroclor 1242, and only half of the congeners present in Aroclor 1254 are also present in Aroclor 1260 (De Voogt et al., 1990). As a result, it can be predicted that dermal absorption may differ among these mixtures. Indeed, studies have shown that more highly chlorinated PCB congeners, as are found in a higher percentage in Aroclor 1260 than in Aroclors 1254 and 1242, have lower oral and dermal bioavailability than lesser chlorinated congeners, particularly when adsorbed to soil particles (Fries et al., 1989; Garner and Matthew, 1998). Thus, it can be expected that dermal uptake of Aroclor 1260 is also lower than that demonstrated for Aroclors 1242 and 1254.

Mayes et al. (2002) Dermal Absorption Study

The Mayes et al. (2002) study, which was sponsored by GE, was designed to address many of the limitations of the Wester et al. (1993) study as they relate to site-specific risk assessments. As such, this study used a methodology similar to that used by Wester et al. (1993) but modified the approach to more closely reflect actual exposures to PCBs in site-specific soils.

The Mayes et al. (2002) study likewise used female Rhesus monkeys. Soil from the Housatonic River floodplain, which did not contain detectable PCBs, was analyzed to contain 20 percent sand, 54 percent silt, and 20 percent clay, with an organic carbon content of 5-6 percent. This soil was sieved to ≤ 150 microns; that sieved fraction contained 8.7 percent organic carbon. This soil was then spiked with radiolabeled Aroclor 1260. To evaluate the potential effects of both soil aging and time of exposure on the bioavailability of the PCBs, this study used both freshly spiked soils and soils that had been aged to simulate weathered PCB soil, and it evaluated absorption that occurred after both 12- and 24-hour exposure periods. Other experimental techniques used in the Mayes et al. (2002) study were similar to those used by Wester et al. (1993).

Using the same procedure as Wester et al. to calculate dermal absorption rates, the calculated mean dermal absorption rates for Aroclor 1260 from soils tested in the Mayes et al. (2002) study ranged from 3.43 to 4.26 percent. The group that was exposed to aged PCBs in soil for 12 hours

had a dermal absorption rate of 3.43 percent. The groups exposed to PCBs in soil for 24 hours had mean absorption rates of 4.07 and 4.26 percent for freshly spiked and aged soils, respectively.

This study demonstrated, using a study protocol very similar to that of Wester et al. (1993), that the dermal absorption rate for Aroclor 1260 from site-specific soils with a higher (and more typical) organic carbon content is substantially lower than the 14 percent estimate derived by Wester et al. (1993) for lower chlorinated PCBs using very low organic carbon content soils. Since the soils and PCB mixture used by Mayes et al. (2002) more closely approximate the conditions at the Housatonic River site, it follows that their results are more representative of PCB dermal absorption from floodplain soils and sediments at this site.

The HHRA recognizes that the Mayes et al. (2002) study used site-specific soils and an Aroclor mixture that more closely resemble the mixtures at this site (Vol. I, p. 2-20 - 2-21; Vol. IIIA, pp. 4-25 - 4-26). However, citing a review by the EPA Superfund Dermal Workgroup (EPA, 2001), the HHRA concludes that two protocol design features preclude the use of this study as the basis for a dermal absorption factor to be used in the HHRA (Vol. I, p. 2-21; Vol. IIIA, p. 4-26). The first feature was that the monkeys were not restrained during the exposure period, as they were in the Wester et al. (1993) study, prompting concern that the lack of restraint could result in loss of soil contact with the skin at the test area and thus lead to a lower than expected applied dose. The second feature was that the study did not control for “monolayer” conditions. This concern is based on the theory that dermal absorption of PCBs comes only from the soil monolayer in immediate direct contact with the skin, and that by using a smaller particle size and the same application rate used by Wester et al. (1993), there was a five-fold excess of soil over that monolayer. According to EPA, correction for that “overloading” would result in an estimated dermal absorption rate of 20 percent for the monolayer, which is higher than EPA’s 14 percent recommendation.

The authors of the Mayes et al. (2002) study do not believe that the lack of restraint had an impact on the study results. As in the Wester et al. (1993) study, the soil was held in place against the clipped skin of the monkeys with a non-occlusive cover that prevented the animals from licking or scratching at the skin. At the 12- and 24-hour time points when the soil application site coverings were removed from the monkeys, it was noted by the experimenters that the soil had by and large remained on the skin as applied, with very little being found “loose” within the occlusion (B.A. Mayes, personal communication). Moreover, restraining non-human primates for 24 hours is a very stressful experimental approach and would have required exceptional measures to gain Institutional

Animal Care and Use Committee approvals. The method used by Mayes et al. (2002) was demonstrated to be adequate for the objectives of the study and avoided the stress of 24-hour restraint.

With respect to the "monolayer" point, EPA's criticism is based on the theory that transfer and absorption occurs only from the soil particles in direct contact with the skin, with no diffusion of PCBs between soil particles, and thus that the monolayer of soil in direct contact with the skin is the only portion of the applied dose that is relevant for calculating absorption. As the EPA Dermal Workgroup itself recognized (EPA, 2001), this monolayer theory has never been validated. Basic physical-chemical principles dictate that diffusion will occur from areas of higher concentration of a solute to areas of lower concentration. The only question is the speed with which the diffusion will occur. Insight into this parameter can be obtained from studies reported by Wester et al. (1990) using PCBs in liquid co-solvents. Wester et al. (1990) reported that Aroclor 1242 applied to skin for 24 hours in mineral oil or trichlorobenzene resulted in absorption of 20.4 and 20.8 percent, respectively, and that Aroclor 1254 applied similarly resulted in absorption of 18.0 and 14.6 percent, respectively. These values (14 to 21 percent) must be higher than the rate of PCB dermal absorption from soil, since the unimpeded diffusion of PCB molecules in a liquid co-solvent would logically be expected to result in a greater absorbed fraction than would occur from a solid matrix, such as soil. Yet the dermal absorption rate calculated by Wester et al. (1993) for a soil loading that, in that study, involved two to three monolayers was nearly as high as those reported for liquid co-solvents. This suggests that absorption did not come only from the monolayer next to the skin, because if it had, the absorption rate calculated for the total soil loading (2-3 monolayers) would have been substantially less than 14 percent. The more likely explanation is that the low organic content of the soil used in Wester et al. (1993) allowed for rapid and complete diffusion and bioavailability, while the soil used in Mayes et al. (2002), with a higher and environmentally relevant organic content, impeded the diffusion of PCBs and thus reduced the bioavailability.

The HHRA further notes (Vol. I, p. 2-21) that the Massachusetts Department of Environmental Protection (MDEP, 2001) also pointed out several shortcomings in the method used by Mayes et al. (2002) to calculate percent absorption. These included the fact that the methodology did not account for distribution of PCBs to various body compartments, which could differ for dermal and intravenous exposures, and that the radiolabeled PCB detected in cage washings, which could have resulted from excretion, were not counted as absorbed. As the HHRA recognizes, however, these same potential shortcomings apply to the Wester et al. (1993) study.

Selection of a Dermal Absorption Factor

While both the Wester et al. (1993) and Mayes et al. (2002) studies have some limitations, the latter used study conditions more closely resembling conditions at the Housatonic River site. In these circumstances, GE believes that a dermal absorption rate of around 4 percent, based on the Mayes et al. (2002) results, is more representative of the level of absorption that is likely to occur after dermal contact with the PCBs found in Housatonic River floodplain soils and sediments, and thus should be used in the HHRA.

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